A Facile Synthesis of 1-Phenylsulfonyl-3-substituted-2-cyanoindoles, 1-Phenylsulfonyl-2-methyl-3-cyanoindoles, and Bifunctional 1-Phenylsulfonylindoles

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Abstract: A facile 'one-pot' introduction of the cyano group into the 2/3-position of indole has been developed from the corresponding aldehydes using anhydrous aluminum chloride and sodium azide.

Key words: indole aldehydes, aluminum chloride, sodium azide, cyanoindoles, bifunctional indoles

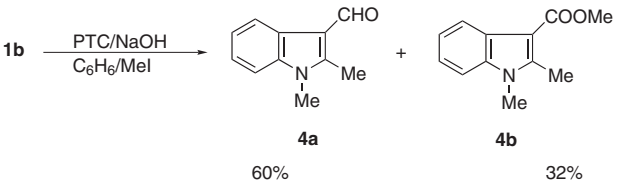
Cyanoindoles are an important class of compounds in pharmacology as some derivatives show antiviral activity,[1,2] they are also used as intermediates in the synthesis of drugs and agrochemicals.[3] Cyanoindoles have been prepared[4] from oximes of indole-3-aldehydes using reagents such as 2,4,6-trichloro-s-triazine, acetic anhydride, and thionyl chloride. 7-Substituted-3-cyanoindoles were reported[5] as starting materials for the synthesis of azepino[3,4,5-*cd*] indole, which is of biological interest. Methyl indole-3-carboxylate has been converted into 3-cyanoindole by sodium bis(trimethylsilyl)amide.[6]

A number of other routes to access cyanoindoles have been developed, such as, the reaction of indole with chlorosulfonyl isocyanate and triethylamine which afforded 3-cyanoindole;[7] the reaction of indole-3-aldehyde with sodium acetate and nitroethane in refluxing acetic acid also gave 3-cyanoindole[5] while treatment of 2- or 3-methylindole with triphenylphosphine thiocyanate (TPPT) yielded[8] the corresponding cyanoindoles in high yield. However, all these routes suffer from some disadvantages.[9,10]

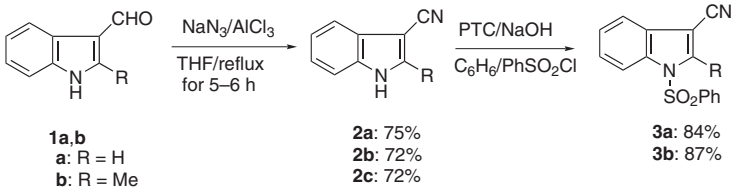
A thorough survey of the literature revealed that the cyano group had been introduced onto benzaldehyde by the reaction of sodium azide and aluminum chloride in boiling THF affording benzonitrile.[11] This reaction was not extended to other aromatic aldehydes. Herein, we wish to report the successful extension of this methodology to indole aldehydes for the synthesis of N-protected cyanoindoles directly, in particular the synthesis of 1-phenylsulfonyl-2-methyl-3-cyanoindole, 1-phenylsulfonyl-3-substituted-2-cyanoindole and their derivatives. We also attempted unsuccessfully to apply these conditions to the synthesis of 2,3-dicyanoindoles.

Our first targets were 3-cyanoindoles; in particular, we looked at the conversion of indole-3-aldehydes[12] into the corresponding 3-cyanoindoles **2a** and **2b**. Treatment with sodium azide and anhydrous aluminum chloride in refluxing anhydrous THF for five to six hours (Scheme 1), furnished **2a** and **2b** in 75% and 72% yields, respectively. Then **2a** and **2b** were converted into their corresponding *N*-phenylsulfonyl derivatives, **3a** and **3b**, under PTC conditions in 84% and 87% yields, respectively.

We were interested in applying this reaction to N-protected indole-3-aldehydes. 2-Methylindole-3-aldehyde (**1b**) underwent N-methylation with excess methyl iodide under PTC conditions to give 1,2-dimethylindole-3-aldehyde[13] (**4a**) in 61% yield and methyl 1,2-dimethylindole-3-carboxylate[14] (**4b**) as a by product in 32% yield (Scheme 2). The ester **4b** probably arises by a Cannizaro type mechanism.



Scheme 2



Scheme 1

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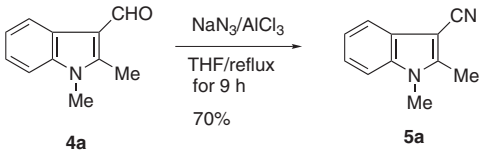
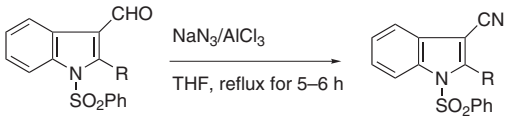
1,2-Dimethylindole-3-aldehyde (**4a**) was converted into 1,2-dimethyl-3-cyanoindole[9] (**5a**) in 65% yield by treatment with sodium azide and aluminum chloride in THF (Scheme 3).



4a **5a**

Scheme 3

Similarly, 1-phenylsulfonyl-3-cyanoindoles, **3a** and **3b**, were synthesized from 1-phenylsulfonylindole-3-aldehydes,[20] **6a** and **6b**, in comparable yields (Scheme 4).



6a,**b**
a: R = H
b: R = Me

3a: 84%
3b: 87%

Scheme 4

The structure of the compound **3b** was confirmed by single crystal X-ray diffraction studies.

Synthetic elaboration of the 2-position of indoles is an area of ongoing interest. We planned to synthesize a variety of 3-substituted-2-cyanoindoles **9a–e** (Cl, Br, SPh, CH_3, CH_2Ph) from 3-substituted-indole-2-aldehydes **8a–e** by the same methodology (Scheme 5). These aldehydes could be prepared from the corresponding 3-substituted-2-bromomethyl-1-phenylsulfonylindoles **7a–e**[15] which, in turn, were prepared from the corresponding 3-sustituted-2-methylindoles in 80–85% yield by a procedure we developed previously (Table 1).[15–19] The structures of compounds **8a**, **8b**, and **8c** were confirmed by single crystal X-ray diffraction studies. All 3-substituted-indole-2-aldehydes **8a–e** were converted into the corresponding 3-substituted-2-cyanoindoles **9a–e** by the procedure described above. The structure of compound **9c** was confirmed by single crystal X-ray diffraction studies. The progress of the reaction was monitored by TLC, which indicated that the formation of 2-cyanoindoles was much slower than the corresponding 3-cyanoindoles.

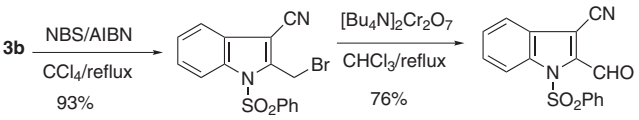
Bifunctional indoles, such as, 1-phenylsulfonyl-3-cyanoindole-2-aldehyde, 1-phenylsulfonyl-2-cyanoindole-3-aldehyde, and 1-phenylsulfonylindole-2,3-dialdehyde have great potential as starting materials for the synthesis of indole alkaloids and medicinally important indole derivatives. Such indoles with two functional groups at both the 2- and 3-positions are not easily accessible.

Table 1 Synthesis of 1-Phenylsulfonyl-3-substituted-cyanoindoles

Compound	R	Indole-2-aldehydes **8**		2-Cyanoindoles **9**	
		Reaction time (h)	Yield (%)	Reaction time (h)	Yield (%)
a	Cl	6	60	6	72
b	Br	5	84	5	80
c	SPh	7	74	8	68
d	CH_3	6	71	7	68
e	CH_2Ph	7	66	9	72

Recently, drugs containing an indole ring have been introduced, which may be due to the fact that an indole ring system may not survive long in vivo due to its facile biodegradation. It is well known that even the essential amino acid tryptophan is degraded and excreted as 3-methylindole. Therefore, a drug with an indole chromophore may not offer severe side effects, which may be promising for this type of bifunctional indoles as useful reagents in combinatorial synthesis.

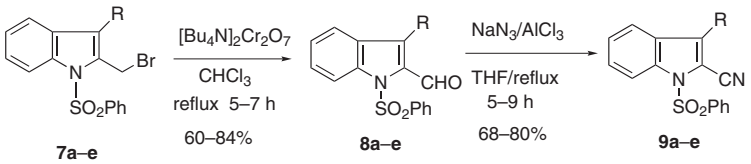
In fact, 1-phenylsulfonyl-3-cyanoindole-2-aldehyde (**11**) was easily synthesized from 1-phenylsulfonyl-2-methyl-3-cyanoindole (**3b**) in two steps (Scheme 6). Smooth allylic bromination of **3b** gave the 1-phenylsulfonyl-2-bromomethyl-3-cyanoindole (**10**) in 93% yield, which was in turn oxidized to **11** in 76% yield. The structure of compound **11** was confirmed by single crystal X-ray diffraction studies.



10 **11**

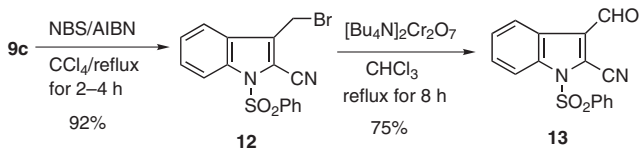
Scheme 6

Similarly the isomeric 1-phenylsulfonyl-2-cyanoindole-3-aldehyde (**13**) was synthesized from the corresponding 1-phenylsulfonyl-2-cyano-3-methylindole (**9c**) via intermediate 1-phenylsulfonyl-3-bromomethyl-2-cyanoindole (**12**), whose structure was confirmed by single crystal X-ray diffraction studies.



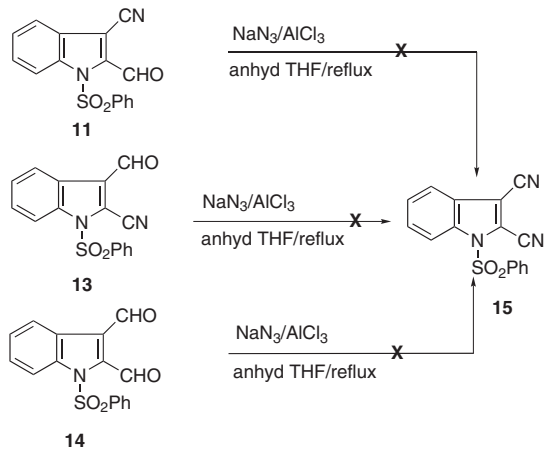
7a–e **8a–e** **9a–e**

Scheme 5



Scheme 7

Finally, we looked at preparing 2,3-dicyanoindole **15** from indole-2,3-dialdehyde **14**.[15] Initially **14** was synthesized from 1-phenylsulfonyl-2,3-dimethylindole, which was converted into 1-phenylsulfonyl-2,3-dibromomethylindole in 87% yield; this was in turn oxidized to **14** in 74% yield. We then attempted to prepare **15** by the methodology described above (Scheme 8). TLC monitoring of the reaction indicated a mixture of products, however, workup of the reaction mixture gave only the starting aldehyde in 70–78% yield. We also attempted to prepare **15** from aldehydes **11** and **13**, but all attempts were in vain. We believe that both functional groups present coordinate with aluminum chloride, thereby preventing attack of sodium azide on the aldehyde group.



Scheme 8

Indole aldehydes were prepared by Vilsmeyer formylation of the corresponding indole by a known procedure.[12] 1-Phenylsulfonylindole-3-aldehyde (**6a**)[20a] and 1-phenyl sulfonyl-2-methylindole-3-aldehyde (**6b**)[20b] were synthesized by known procedures; analytical data were in agreement with those previously published. Bromination of cyanoindoles was adopted from the published procedure;[18] the reaction was carried out on a 5 mmol scale with one equivalent of NBS.

^{1}NMR spectra were recorded on Bruker DPX (200 MHz), Bruker (300 MHz), Jeol GSX (400 MHz), Jeol FX (90 MHz) and Varian (90 MHz) instruments with TMS as the internal standard. Mass spectra were recorded on a Jeol-JMS-DX-303HF instrument under 70 eV. IR spectra were recorded with a Shimadzu 8300 FT-IR spectrometer. Elemental analyses were performed on a Perkin Elmer series II CHNS/O Analyzer. All the melting points are uncorrected. Acme 200 mesh silica gel was thoroughly washed with distilled water and oven-dried at 150 °C prior to use. All solvents were purified by standard methods.

N-Methylation of 2-Methylindole-3-aldehyde under PTC Conditions

To a solution of 2-methylindole-3-aldehyde (1.59 g, 10 mmol) in benzene (50 mL) and a 50% solution of NaOH (50 mL), tetrabutylammonium hydrogen sulfate (100 mg) and MeI (20 mmol) in benzene were added. The mixture was stirred for 2 h, poured over crushed ice (75 g), and extracted with EtOAc (3 × 50 mL). The organic layer was separated, washed with H_2O (3 × 25 mL), and dried ($MgSO_4$). Removal of the solvent under reduced pressure followed by column chromatography (EtOAc–hexane, 2: 8) gave **4a** and **4b**.

1,2-Dimethylindole-3-aldehyde (4a)

Yield: 1.04 g (61%); mp 125 °C (Lit.[13] 126 °C).

IR (KBr): 1643 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.66 (s, 3 H, CH_3), 3.68 (s, 3 H, NCH_3), 7.26–7.29 (m, 3 H, ArH), 8.24–8.26 (m, 1 H, indole-7H), 10.14 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.53, 29.58, 109.10, 109.13, 114.18, 120.80, 122.74, 123.04, 125.67, 136.93, 147.68, 184.05.

Methyl 1,2-Dimethylindole-3-carboxylate (4b)

Yield: 0.64g (32%); mp 141 °C (Lit.[14] 140 °C).

3-Cyanoindoles from Indole-3-aldehydes; General Procedure

To a stirred solution of anhyd $AlCl_3$ (2.70 g, 20 mmol) in anhyd THF (100 mL), NaN_3 (3.90 g, 60 mmol) and indole-3-aldehyde (10 mmol) were added and the resulting reaction mixture was refluxed. The progress of the reaction was monitored by TLC. The suspension gradually turned pale yellow after 5–6 h. When the reaction was complete excess THF was removed by distillation and the residue was diluted with 10% HCl (10 mL). The aqueous layer was extracted with $CHCl_3$ (2 × 50 mL), the organic layer was separated, and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was purified by column chromatography (EtOAc–hexane, 2:8) to give 3-cyanoindoles in 70–87% yield.

N-Phenylsulfonylation of 3-Cyanoindoles

To a solution of 3-cyanoindole (10 mmol) in benzene (50 mL) and a 50% solution of NaOH (25mL), tetrabutylammonium hydrogen sulfate (100 mg) and $PhSO_2Cl$ (1.25 mL, 10 mmol) in benzene were added in one portion. The reaction mixture was stirred for 5–6 h, poured over crushed ice (75 g), and extracted with EtOAc (3 × 50 mL). The organic layer was separated, washed with H_2O (3 × 35 mL), and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by column chromatography (EtOAc–hexane, 2:8) to give *N*-phenylsulfonyl-3-cyanoindoles.

3-Cyanoindole (2a)

Yield: (75%); mp 183 °C (Lit.[7] 183–184 °C).

IR (KBr): 3213, 2221 cm^{-1}.

2-Methyl-3-cyanoindole (2b)

Yield: 1.12g (72%); mp 204 °C (Lit.[8] 204–206 °C).

IR (KBr): 3236, 2213 cm^{-1}.

MS: *m*/*z* (%) = 156 (M^+, 9), 155 (22), 141 (57), 128 (9), 78 (9), 77 (100), 51 (14).

1,2-Dimethyl-3-cyanoindole (5a)

Yield: 1.19 g (70%); mp 103 °C (Lit.[8] 104–105 °C).

1-Phenylsulfonyl-3-cyanoindole (3a)

Yield: 2.02 g (84%); mp 151–152 °C.

IR (KBr): 2224, 1385, 1176 cm^{-1}.

MS: *m*/*z* (%) = 282 (M^+, 18), 141 (51), 114 (34), 80 (100).

1-Phenylsulfonyl-2-methyl-3-cyanoindole (3b)
Yield: 2.57 g (87%); mp 154 °C.

IR (KBr): 2233, 1388, 1180 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.81 (s, 3 H, CH_3), 7.26–7.87 (m, 8 H, ArH), 8.20–8.22 (d, *J* = 9 Hz, 1 H, indole-7H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.80, 94.63, 113.86, 114.51, 119.10, 124.76, 125.84, 126.49, 126.80, 129.66, 134.66, 135.38, 138.04, 146.07.

MS: *m/z* (%) = 296 (M^+, 11), 278 (10), 256 (10), 183 (22), 167 (25), 154 (76), 148 (44), 142 (11), 114 (18), 90 (49), 81 (30) 72 (38), 69 (54), 57 (100), 56 (14.0).

Anal. Calcd for $C_{16}H_{12}N_2O_2S$: C, 64.86; H, 4.05; N, 9.46. Found: C, 64.49; H, 3.92; N, 9.24.

1-Phenylsulfonyl-3-substituted-indole-2-aldehydes 8; General Procedure
To a solution of 1-phenylsulfonyl-2-bromomethyl-3-substituted indole (5 mmol) in anhyd $CHCl_3$ (60 mL), bistetrabutylammonium dichromate[21] (5.0 mmol) was added. The resulting solution was refluxed for 8 h. The reaction mixture was filtered through a plug of celite or silica gel (10 g) to remove inorganic material and unreacted tetrabutylammonium salts. The celite or silica gel was washed with Et_2O (75 mL). The ethereal residues were dried ($MgSO_4$), the solvent was removed, and the residue was purified by column chromatography (hexane–EtOAc, 7:3) to afford the appropriate indole-2-aldehyde as a pure crystalline solid in 60–84% yield.

1-Phenylsulfonyl-3-chloroindole-2-aldehyde (8a)
Yield: 0.91g (60%); mp 154 °C.

IR (KBr): 1677, 1357, 1176 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.79 (m, 8 H, ArH), 8.25–8.27 (d, *J* = 8.0 Hz, 1 H, indole-7H), 10.49 (s, 1 H, CHO).

MS: *m/z* (%) = 321 (M + 2, 7), 319 (M^+, 15), 178 (20), 150 (18), 140 (30), 122 (17), 114 (17), 84 (100), 51 (45).

1-Phenylsulfonyl-3-bromoindole-2-aldehyde (8b)
Yield: 1.52g (84%); mp 172 °C.

IR (KBr): 1674, 1367, 1186 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.24–7.78 (m, 8 H, ArH), 8.22–8.27 (d, *J* = 10.0 Hz, 1 H, indole-7H), 10.42 (s, 1 H, CHO).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 111.89, 115.53, 122.32, 125.36, 126.82, 129.00, 129.29, 130.09, 132.16, 134.44, 137.07, 181.96.

MS: *m/z* (%) = 365 (M + 2, 4), 363 (M^+, 4), 224 (27), 196 (33), 169 (26), 141 (73), 114 (100), 77 (6).

1-Phenylsulfonyl-3-phenylthioindole-2-aldehyde (8c)
Yield: 1.45g (74%); mp 118 °C (Lit.[15] 120 °C).

1-Phenylsulfonyl-3-methylindole-2-aldehyde (8d)
Yield: 1.06g (71%); mp 206 °C (Lit.[18] 208 °C).

1-Phenylsulfonyl-3-benzylindole-2-aldehyde (8e)
Yield: 1.24 g (66%); mp 123 °C (Lit.[19] 124 °C).

1-Phenylsulfonyl-3-substitute-2-cyanoindoles; General Procedure
The procedure was exactly the same as that described for 3-cyanoindoles except the procedure was carried out on a 10 mmol scale.

1-Phenylsulfonyl-3-chloro-2-cyanoindole (9a)
Yield: 0.53g (72%); mp 206 °C.

IR (KBr): 2224, 1378, 1186 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.18–7.98 (m, 8 H, ArH), 8.11–8.14 (d, *J* = 9.0 Hz, 1 H, indole-7H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 115.34, 117.86, 124.00, 125.13, 127.16, 129.57, 131.48, 134.67, 136.54, 141.37, 158.67.

Anal. Calcd for $C_{15}H_9N_2O_2SCl$: C, 56.88; H, 2.84; N, 8.85. Found: C, 57.08; H, 2.69; N, 8.57.

1-Phenylsulfonyl-3-bromo-2-cyanoindole (9b)
Yield: 0.722 (80%); mp 188–190 °C.

IR (KBr): 2221, 1373, 1180 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.27–8.06 (m, 8 H, ArH), 8.24–8.27 (d, *J* = 9.0 Hz, 1 H, indole-7H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 109.14, 114.65, 121.46, 124.88, 125.36, 126.56, 127.58, 128.43, 129.46, 129.79, 135.03, 157.64.

MS: *m/z* (%) = 362 (M + 2, 22), 360 (M^+, 20), 219 (26), 141 (94), 113 (21), 84 (100), 62 (18), 51 (99).

Anal. Calcd for $C_{15}H_9N_2O_2SBr$: C, 49.86; H, 2.49; N, 7.76. Found: C, 50.12; H, 2.55; N, 7.71.

1-Phenylsulfonyl-3-phenylthio-2-cyanoindole (9c)
Yield: 0.69g (68%); mp 120 °C.

IR (KBr): 2110, 1371, 1175 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.95–7.89 (m, 13 H, ArH), 8.19–8.22 (d, *J* = 12.0 Hz, 1 H, indole-7H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 70.54, 115.10, 117.86, 121.16, 123.06, 124.69, 126.19, 126.97, 127.45, 128.39, 129.21, 129.59, 130.53, 133.53, 135.15, 136.52, 137.55.

MS: *m/z* (%) = 391(M^+, 7), 350 (14), 284 (3), 244 (9), 209 (26), 163 (21), 128 (74), 101 (35), 84 (100), 51 (80).

1-Phenylsulfonyl-3-methy-2-cyanoindole (9d)
Yield: 0.50g (68%); mp 182–184 °C.

IR (KBr): 2233, 1378, 1175 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, CH_3), 7.26–8.00 (m, 8 H, ArH), 8.19–8.21 (d, *J* = 12.0 Hz, 1 H, indole-7H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.12, 114.76, 120.73, 124.48, 127.06, 128.69, 128.86, 129.53, 134.50.

MS: *m/z* (%) = 296 (M^+, 31), 231 (5), 155 (56), 141 (44), 128 (18), 101 (9), 84 (100).

Anal. Calcd for $C_{16}H_{12}N_2O_2S$: C, 64.86; H, 4.05; N, 9.46. Found: C, 65.15; H, 3.78; N, 9.05.

1-Phenylsulfonyl-3-benzyl-2-cyanoindole (9e)
Yield: 0.70g (72%) mp 120 °C.

IR (KBr): 2102, 1367, 1173 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.79 (s, 2 H, CH_2), 7.23– 8.16 (m, 13 H, ArH), 8.17– 8.20 (d, *J* = 9.0 Hz, 1 H, indole-7H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 105.92, 114.83, 120.34, 120.41, 121.15, 124.50, 125.23, 126.73, 127.02, 128.22, 129.01, 129.25, 129.31, 131.21, 132.75, 134.23, 135.77, 138.01.

Anal. Calcd for $C_{22}H_{16}N_2O_2S$: C, 70.96; H, 4.30; N, 7.52. Found: C, 71.22; H, 4.13; N, 7.17.

1-Phenylsulfonyl-2-bromomethyl-3-cyanoindole (10)
Yield: 1.74g (93%); mp 144 °C.

IR (KBr): 2234, 1372, 1183 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.14 (s, 2 H, CH_2), 7.26–8.11 (m, 8 H, ArH), 8.23–8.25 (d, *J* = 8.0 Hz, 1 H, indole-7H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.21, 97.07, 112.62, 114.95, 120.14, 125.36, 126.56, 127.03, 127.36, 127.47, 129.87, 135.05, 135.65, 137.57, 144.01.

MS: *m*/*z* (%) = 376 (M + 2, 52), 374 (M^+, 56), 297 (79), 232 (62), 203 (44), 179 (55), 154 (79), 141(83), 127 (89), 117 (39), 100 (53), 84 (100), 57 (40).

Anal. Calcd for $C_{16}H_{11}N_2O_2SBr$: C, 51.20; H, 2.93; N, 7.47. Found: C, 50.80; H, 2.85; N, 7.44.

1-Phenylsulfonyl-3-bromomethyl-2-cyanoindole (12)
Yield: 1.72 g (92%); mp 144 °C.

IR (KBr): 2213, 1372, 1179 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.66 (s, 2 H, CH_2), 7.25–8.04 (m, 8 H, ArH), 8.21–8.23 (d, *J* = 8.0 Hz, 1 H, indole-7H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.80, 107.55, 110.94, 114.87, 121.10, 126.51, 127.29, 129.42, 129.87, 132.56, 135.06, 136.80, 137.31.

MS: *m*/*z* (%) = 376 (M + 2, 11), 374 (M^+, 12), 295 (58), 235 (5), 154 (100), 141 (79), 127 (19), 115 (4), 102 (23), 84 (92), 51 (35).

Anal. Calcd for $C_{16}H_{11}N_2O_2SBr$: C, 51.20; H, 2.93; N, 7.47. Found: C, 50.90; H, 2.92; N, 7.42.

1-Phenylsulfonyl-3-cyanoindole-2-aldehyde (11)
Synthesized, on a 5 mmol scale with bistetrabutylammonium dichromate (1 equiv), by a similar procedure used for the preparation of **8**.

Yield: 1.84 g (76%); mp 160 °C.

IR (KBr): 2231, 1669, 1370, 1182 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.82 (m, 8 H, ArH), 8.22–8.24 (d, *J* = 10.0 Hz, 1 H, indole-7H), 10.42 (s, 1 H, CHO).

MS: *m*/*z* (%) = 310 (M^+, 17), 282 (8), 228 (6), 190 (5), 170 (55), 141 (77), 114 (100), 84 (100).

1-Phenylsulfonyl-2-cyanoindole-3-aldehyde (13)
Synthesized, on a 5 mmol scale with bistetrabutylammonium dichromate (1 equiv), by a similar procedure used for the preparation of **8**.

Yield: 1.72 g (75%); mp 308 °C.

IR (KBr): 2231, 1672, 1378, 1181 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 –8.05 (m, 8 H, ArH), 8.26–8.28 (d, *J* = 8.0 Hz, 1 H, indole-7H), 10.26 (s, 1 H, CHO).

1-Phenylsulfonylindole-2,3-dialdehyde (14)
Synthesized, on a 5 mmol scale with bistetrabutylammonium dichromate (2 equiv), by a similar procedure used for the preparation of **8**.

Yield: 1.15g (74%); mp 158 °C (Lit.[18] 160 °C).

IR (KBr): 1665, 1372, 1185 cm^{-1}.

Attempted Synthesis of 1-Phenylsulfonyl-2,3-dicyanoindole (15)
To a stirred solution of anhyd $AlCl_3$ (1.35 g, 10 mmol) and NaN_3 (1.95 g, 30 mmol) in anhyd THF (50 mL), bifunctional indole-aldehyde (**11**/**13**, 5 mmol), was added and the resulting solution was heated at gentle reflux for 6–9 h (with bisaldehyde **14**, twice the amount of reagents were added). The reaction was monitored by TLC, which indicated a mixture of products. The excess THF was removed and the residue was diluted with 10% HCl (5 mL). The aqueous layer was extracted with $CHCl_3$ (2 × 25mL). The organic layer was separated, dried over anhyd Na_2SO_4, and concentrated under reduced pressure to give the starting bifunctional indole-aldehydes, which were identified by their mp and IR spectra; yield: 70–78%.

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